

In the Claims

Please amend the claims as follows:

1. (Original) An isolated and purified DNA molecule comprising a human genomic DNA segment encoding TLR4, a biologically active fragment or variant thereof.
2. (Original) The DNA molecule of claim 1 wherein the DNA segment encodes a variant TLR4.
3. (Original) The DNA molecule of claim 2 wherein the variant TLR4 has at least one amino acid substitution in the extracellular domain of TLR4.
4. (Original) The DNA molecule of claim 3 wherein the variant TLR4 comprises a glycine residue at position 299 or an isoleucine residue at position 399.
5. (Original) An isolated and purified nucleic acid molecule comprising a human nucleic acid segment encoding a variant TLR4, or a biologically active fragment thereof.
6. (Original) The nucleic acid molecule of claim 5 wherein the variant has at least one amino acid substitution in the extracellular domain of TLR4.
7. (Original) The nucleic acid molecule of claim 6 wherein the variant comprises a glycine residue at position 299 or an isoleucine residue at position 399.
8. (Original) An expression cassette comprising a promoter operably linked to a human DNA segment encoding a variant TLR4, or a biologically active fragment thereof.
9. (Original) The expression cassette of claim 8 wherein the variant TLR4 has at least one amino acid substitution in the extracellular domain of TLR4.

10. (Original) The expression cassette of claim 8 wherein the variant TLR4 comprises a glycine residue at position 299 or an isoleucine residue at position 399.
11. (Original) A host cell, the genome of which is augmented by the DNA molecule of claim 1.
12. (Original) A host cell, the genome of which is augmented by the nucleic acid molecule of claim 5.
13. (Original) A method to prepare a variant TLR4, comprising: culturing a host cell transformed with the nucleic acid molecule of claim 5 operably linked to a promoter, so that said host cell expresses the variant TLR4.
14. (Original) A method to prepare a variant TLR4, comprising: culturing a host cell transformed with the DNA molecule of claim 1 operably linked to a promoter, so that said host cell expresses the variant TLR4.
15. (Original) The method of claim 13 or 14 further comprising isolating TLR4 from the host cell.
16. (Currently Amended) A method of identifying a human at risk of, or having, an indication associated with altered innate immunity, comprising:
 - a) contacting an amount of ~~DNA~~ nucleic acid obtained from a human physiological sample with an amount of at least one Toll-like receptor-4 (TLR4)-specific TLR4-specific oligonucleotide under conditions effective to amplify ~~the~~ TLR4 DNA having SEQ ID NO:62, the complement thereof, or a portion thereof, so as to yield amplified TLR4 DNA which includes DNA encoding amino acid residue 299 or 399 of TLR4, wherein the TLR4-specific oligonucleotide comprises at least two nucleotide substitutions which

result in a restriction site that is indicative of nucleic acid that encodes a TLR4 polypeptide with an amino acid substitution at residue 299 or 399; and

b) detecting or determining whether the amplified DNA encodes ~~at least a portion of a variant~~ TLR4 polypeptide having an amino acid substitution at residue 299 or 399, thereby identifying whether the human is at risk of or has an indication associated with innate immunity.

17. (Currently Amended) The method of claim 16 or 28 wherein the nucleic acid sample comprises genomic DNA.
18. (Currently Amended) The method of claim 16 or 28 wherein the nucleic acid sample is cDNA.
19. (Currently Amended) The method of claim 16 or 28 wherein the amplified DNA is subjected to electrophoresis in step b).
20. (Original) Isolated, variant human TLR4 polypeptide, or a biologically active fragment thereof.
21. (Original) The isolated polypeptide of claim 20 wherein the variant TLR4 has at least one amino acid substitution in the extracellular domain of TLR4.
22. (Original) The isolated polypeptide of claim 21 wherein the variant TLR4 comprises a glycine residue at position 299 or an isoleucine residue at position 399.
23. (Original) A method to identify an agent that alters TLR4 activity, comprising:
 - a) contacting a mammalian cell which expresses TLR4 with the agent; and
 - b) detecting or determining whether the agent alters TLR4 activity.

24. (Original) The method of claim 23 wherein the mammalian cell is transformed with a recombinant nucleic acid molecule encoding human TLR4.
25. (Original) An agent identified by the method of claim 24.
26. (Original) A method to alter TLR4 activity, comprising: contacting a mammalian cell with an agent effective to alter TLR4 activity.
27. (Original) The method of claim 26 wherein the mammalian cell is a human cell.
28. (Currently Amended) A method to detect a polymorphism in a human TLR4 gene, comprising: detecting or determining whether ~~a nucleic acid sample~~ amplified TLR4 DNA obtained from a human nucleic acid sample comprises nucleic acid encoding a ~~variant~~ TLR4 polypeptide having an amino acid substitution at residue 299 or 399 of TLR4, wherein the amplified TLR4 DNA is obtained by contacting an amount of the nucleic acid sample with an amount of at least one TLR4-specific oligonucleotide under conditions effective to amplify TLR4 DNA having SEQ ID NO:62, the complement thereof, or a portion thereof, and wherein the TLR4-specific oligonucleotide comprises at least two nucleotide substitutions which result in a restriction site that is indicative of DNA that encodes a TLR4 polypeptide with an amino acid substitution at residue 299 or 399.
29. (Original) A transgenic mouse whose cells comprise a chimeric DNA sequence, wherein the chimeric DNA sequence comprises a DNA segment encoding human TLR4, wherein the chimeric DNA sequence is integrated into the genome of the cells of the mouse, and wherein the DNA segment is expressed in the transgenic mouse so as to result in the transgenic mouse exhibiting altered innate immunity relative to a corresponding nontransgenic mouse.

30. (Original) The transgenic mouse of claim 29 wherein the DNA segment encodes a variant human TLR4.
31. (Canceled).
32. (Currently Amended) The method of claim ~~31~~ 16 or 28 wherein the nucleic acid in the sample DNA encodes a ~~variant TLR4~~ having an amino acid substitution at residue 299.
33. (Currently Amended) The method of claim ~~31~~ 16 or 28 wherein the oligonucleotide comprises SEQ ID NO:66 or SEQ ID NO:67.
34. (Currently Amended) The method of claim ~~31~~ 16 or 28 wherein the nucleic acid in the sample DNA encodes a ~~variant TLR4~~ having an amino acid substitution at residue 399.
35. (Currently Amended) The method of claim ~~31~~ 16 or 28 wherein the oligonucleotide comprises SEQ ID NO:68 or SEQ ID NO:69.
36. (New) The method of claim 32 wherein the substitution at residue 299 is glycine for aspartic acid.
37. (New) The method of claim 34 wherein the amino acid substitution at residue 399 is isoleucine for threonine.
38. (New) The method of claim 16 or 28 wherein at least two TLR4 specific oligonucleotides are contacted with the sample.
39. (New) The method of claim 38 wherein one of the TLR4 specific oligonucleotides is SEQ ID NO:12, SEQ ID NO:18, SEQ ID NO:24, SEQ ID NO:30, SEQ ID NO:36, SEQ ID NO:42, SEQ ID NO:48, SEQ ID NO:54, SEQ ID NO:13, SEQ ID NO:19, SEQ ID

NO:25, SEQ ID NO:31, SEQ ID NO:37, SEQ ID NO:43, SEQ ID NO:49, SEQ ID NO:55, SEQ ID NO:14, SEQ ID NO:20, SEQ ID NO:26, SEQ ID NO:32, SEQ ID NO:38, SEQ ID NO:44, SEQ ID NO:50, SEQ ID NO:56, SEQ ID NO:15, SEQ ID NO:21, SEQ ID NO:27, SEQ ID NO:33, SEQ ID NO:39, SEQ ID NO:45, SEQ ID NO:51, SEQ ID NO:57, SEQ ID NO:16, SEQ ID NO:22, SEQ ID NO:28, SEQ ID NO:34, SEQ ID NO:40, SEQ ID NO:46, SEQ ID NO:52, SEQ ID NO:58, SEQ ID NO:17, SEQ ID NO:23, SEQ ID NO:29, SEQ ID NO:35, SEQ ID NO:41, SEQ ID NO:47, SEQ ID NO:53 or SEQ ID NO:59.